NICE technology appraisal – nasal continuous positive airway pressure for the treatment of obstructive sleep apnoea. Submission from British Thoracic Society

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1.0 Definition of Obstructive Sleep Apnoea Syndrome.

Obstructive sleep apnoea (OSA) is a condition where the upper airway, behind the tongue, repeatedly narrows or collapses during sleep[1]. This leads to recurrent asphyxia and micro-arousals that greatly disturb sleep[2]. In most cases the patient is being awoken over 300 times a night, is unaware of this sleep fragmentation, and as a consequence is unaccountably sleepy and tired during the day[3]. This reduces vigilance and concentration, leading to poor performance in a number of areas, in particular while driving[4], but also at work and in the home. When combined with such symptoms, it is usually called sleep apnoea *syndrome*. There are a number of causes, but the majority are either due to increased tissue bulk in the neck (either fat or muscle) [5], or crowding of the upper airway from subtle variations of the lower facial structure [6], or both. One third of sufferers in the UK are not obese (BMI>30). Rarer causes include tonsillar hypertrophy, hypothyroidism, and acromegaly for example.

2.0 Prevalence

The prevalence depends on the exact definition of the syndrome but various studies estimate that in the UK about 0.5 to 1% of middle aged men have a moderate to severe form [7;8], with the prevalence in women being about a quarter of this. Thus the best estimates suggest that there are about 200,000 sufferers who would benefit from treatment, with only about 25,000 (13%) identified so far. The prevalence is higher in the US due to higher levels of overweight. The general tendency for an increase in BMI levels in western cultures is leading to an increased prevalence of OSA, in a similar way to type II diabetes. Indeed the prevalence of OSA and type II diabetes probably go hand in hand with about a quarter of such patients having OSA as well as their type II diabetes[9]

3.0 Prognosis and Complications

OSA is essentially a lifelong condition unless there is treatment or an alteration in the relevant risk factors. The average age of presentation in most clinics is around 50, with a range from 30 to 80 [10;11]. The disorder occurs in children, but the usual cause is adeno-tonsillar hypertrophy [12]. Various cross sectional studies have shown an association between OSA and cardiovascular disease [13;14], but the exact contribution to cardiovascular morbidity is unclear. There is no doubt that moderate to severe OSA produces significant hypertension, reversible with treatment [15-18], and uncontrolled intervention studies show reduced cardiovascular mortality with treatment [19;20]. However, there is slightly better evidence for road traffic accidents,

and OSA raises such accident rates about 5 to 7 times over control rates [21]: and this reverses to normal levels with diagnosis and treatment [22].

4.0 Levels of disability

The level of disability in patients with OSA has been estimated by a number of groups [10;11;23-28]. Standard measures of 'quality of life' or 'self reported health status', such as the SF36, show considerably reduced levels, particularly in the dimensions assessing 'energy and vitality'. The QALY (quality adjusted life year) reduction due to OSA has been estimated to be about 10% (where death is 100%) [29]. Many of these patients also fail at work and at home with reductions in income and deterioration in personal relationships.

5.0 Current treatment options

5.1 Nasal continuous positive airway pressure

The only fully effective treatment for OSA is nasal continuous positive airway pressure (CPAP), invented in the early 80's by Colin Sullivan[30]. This involves wearing a small mask over the nose (sometimes nose and mouth) during sleep, supplied with air from a pump, that slightly raises the pressure in the pharynx, thus splinting it open and returning breathing to normal [30]. The obstructions resolve, the sleep returns to normal, and the daytime sleepiness disappears [11;31]. Although CPAP is a cumbersome and unattractive therapy, patients use it for, on average, over 5 hours per night because of its obvious symptomatic benefits [24;32]. At present it is estimated that only about 25,000 out of the probable 200,000 patients with OSA in the UK are on nasal CPAP. This is due to a combination of lack of recognition and a lack of facilities for diagnosis and treatment.

Nasal CPAP machines are all essentially similar. They deliver a fixed pressure throughout the night, titrated to be the minimum necessary to maintain upper airway patency. The pressure required can be established via a number of different techniques, including the use of machines that automatically 'hunt' the pressure required on a continuous basis. Different manufacturers have added a variety of extra features, but essentially the devices still deliver a splinting pressure to the airway. There is currently no evidence of superiority of one manufacturers CPAP machine over any other for routine use. There is some preliminary evidence that in patients requiring somewhat higher pressures than average, then machines that either continually hunt the pressure, or back-off slightly on the pressure during expiration , may be more comfortable and minimally improve compliance, but they are not more efficacious [33-35]. Thus at present all CPAP machines should be considered of equal efficacy.

5.2 Weight loss

In those subjects who are overweight, then weight loss is an option, but in OSA weight loss is particularly difficult, and sleep clinics are no better at persuading patients to lose weight than are diabetic and cardiovascular clinics [36]. Obesity surgery may be a viable option for a small subset of patients, but facilities for this in the UK are severely limited (NICE technology appraisal guidance no. 46).

5.3 Mandibular advancement devices

Because relative retrognathia is a cause in some individuals, the use of a mandibular advancement device, worn in the mouth at night, can be effective [37;38]. However the benefits are unpredictable, and on average less successful [39]. They are no cheaper than nasal CPAP, and indeed are probably more expensive due to the need for regular dental follow-up and device replacement. They are therefore second line therapy in patients with symptomatic OSA, but are appropriate for the control of snoring where there is evidence of efficacy.

5.4 Surgery

Although popular in the 80s and early 90s, surgery to the pharynx is rarely appropriate or effective, except when there are large tonsils [40]. A recent Cochrane review concluded that there was no evidence to support surgery for OSA, and agrees with other evidenced based reviews [41;42].

6.0 What is the evidence for efficacy of CPAP?

Despite much evidence for efficacy, there is still scepticism about the use of nasal CPAP for OSA. The concept of CPAP is extremely simple, but developing systems that are as comfortable as possible and acceptable to patients has been difficult. There is good evidence that the provision of the equipment to a patient is not enough on its own, but requires an education and continuing support package to derive the best outcomes [43]. Nasal CPAP was first described in 1981 [30], and has been increasingly available since that time as more companies have designed and built suitable machines and masks for home use. They are now widely available from a number of companies, and UK prices are some of the lowest in the world. When purchased in bulk by departments treating large numbers of patients, a nasal CPAP pump costs little over £200, and they last about 7 years. The masks cost between £70 and £120 and last about 6 to 12 months.

There is good evidence that nasal CPAP is the best treatment for OSA and is the standard therapy against which others are judged. As detailed in the section below, the effects on quality of life are some of the largest ever measured.

The marked effect of nasal CPAP on patients with OSA led to its introduction through the 80s and 90s without any randomised placebo controlled trials demonstrating efficacy. The sole evidence base consisted of case series. In 1997 an evidence based review [44] pointed out this lack of controlled data and stimulated several centres to do formal controlled trials [11;23;26;45-47]. There are now many proper randomised trials that have used either supportive care, a tablet placebo, or nasal CPAP with a low pressure (that does not abolish the OSA) to act as a control. All these trials (involving hundreds of patients) have demonstrated large effect sizes using various endpoints such as subjective and objective sleepiness, simulated driving ability [46], and blood pressure. We assume these studies will provide the evidence upon which NICE will base its conclusions. In addition when quality of life questionnaires (e.g. SF 36) have been used, the improvements seen are greater than those for any other treatment for any other condition so far studied in this way. The number needed to treat is only 1.4 [11]. One such trial treated moderate to severe cases of OSA and randomised to either full nasal CPAP treatment (n=50) or placebo nasal CPAP (that

neither improved nor worsened the OSA, n=51). Compared to placebo, there were large improvements in subjective sleepiness (effect size 2.2), objectively measured sleepiness (effect size 0.70), and SF 36 scores (energy and vitality dimension, effect size 1.7) [11]. There have now been several systematic evidence-based reviews by reputable organisations (including Cochrane and SIGN), all of which have concluded that nasal CPAP for OSA is extremely valuable with large treatment effects [29;40;48-51].

There have been historical control, and case control, studies looking at the effects of nasal CPAP in OSA on car accident rates and overall health costs. For example, the accident rate in patients with OSA was three times the control population level during the three years to diagnosis and this fell to control levels over the three years post diagnosis [22]. It has been estimated that treating 500 patients for 5 years would prevent 1 fatal accident, 75 injury accidents, and 224 property damage accidents. Using current DT figures for the costs of accidents this would save £5.3 million against an estimated treatment cost of £0.4 million [52].

Two studies have looked at the health costs incurred in the years before and after the diagnosis of OSA was made (and nasal CPAP treatment given), compared to those in a matched control group [53;54]. It appears that these patients are presenting for above average numbers of health interventions before diagnosis, and return to baseline after treatment.

Finally there are randomised placebo-controlled trial data showing that blood pressure, both during the night and the day, is reduced by nasal CPAP therapy in patients with OSA, particularly in those with more severe disease and those on anti-hypertensive agents [15-18]. The fall in blood pressure would be predicted to have a significant effect on the 5 and 10 year cardiovascular adverse event rate [15], but no long term interventional trials have been done to confirm this.

7.0 Why the NICE technology appraisal is important

The commissioning of health care has become increasingly guided by evidence of effectiveness and cost effectiveness, and correctly so. Many organisations exist to review the evidence and provide guidance for purchasers. However, the National Institute for Excellence has become the most powerful guide for purchasers, alongside the National Service Frameworks. Such is the nature of health care purchasing, that treatments not reviewed by NICE, or included in NSFs, are at a severe disadvantage. Where treatments are established, and their requirement for funding is not increasing, then the absence of a NICE guideline is not too disadvantageous. However, in a relatively new area, which is expanding due to greater knowledge and awareness, the absence is a severe impediment to the establishment of much needed services. Even a treatment such as nasal CPAP for OSA, with its extensive evidence base, is at a disadvantage compared to the extensive coverage of cancer drugs, for example. The manufacturers who make CPAP machines do not have the financial and political weight of the pharmaceutical industries, and therefore there has not been the fast tracking and early NICE appraisals of CPAP, as there have been in the world of cancer and cardiovascular disease.

Although there is as yet no NICE guidance, in 2003 SIGN (Scottish Intercollegiate Guidelines Network) published on OSA [40] and their work was

endorsed by the BTS (British Thoracic Society). In 2001, the Cochrane collaboration reviewed nasal CPAP [48]. In 2000, the Australian MRC also reviewed nasal CPAP [50]. More recently the American Academy of Sleep Medicine has published its view [51].

Finally, the recent devolution of health care purchasing to PCTs, over the last few years, has led to a dilution of the expertise on priorities in health care that was available to the previous Health Authorities. More than ever, those responsible for choices about purchasing rely on authoritative central guidance. There are many areas in the country where ignorance of OSA and its treatment, and the absence of a NICE appraisal, have led to a reduction in, and sometimes withdrawal of, sleep apnoea services. There is real 'post code availability' of OSA services. Despite this patchy purchasing, the number of referrals to respiratory departments for the investigation and treatment of OSA continues to rise. For example the Oxford unit now receives over 30 referrals a week and puts 12 to 16 new patients on nasal CPAP a week, with increasing referrals from new areas that are now failing to purchase such services locally.

In order to investigate this variability in services, the BTS recently commissioned a survey of its consultant members as to the availability of OSAS services. In summary, 40% of hospitals had no service at all, over half of whom had tried to establish services but had been unable to do so. Of those with a service, 30% are unable to deliver a CPAP service, and only perform diagnostic studies. Thus only 40% of the hospitals surveyed were able to provide a service for both diagnosis and treatment. Over 30% of the hospitals with a service had delays of over 6 months from referral to treatment due to resource limitations.

The BTS also contacted the commissioning departments of 51 PCTs to establish their approach to purchasing sleep apnoea and CPAP services. Of 51 PCTs contacted 28 either failed to respond, or to answer simple questions on their commissioning arrangements for this condition. Of the 23 who replied, 11 were not aware of a service. Only 10 were currently commissioning a service, 6 on a regular basis and the others ad hoc, on a case by case basis.

The conclusions from these surveys are that provision across the country is highly variable from satisfactory to non-existent. Thus there is urgent need for a NICE appraisal in order to guide purchasers and deliver a uniform service across the country.

8.0 Can the UK health services cope with an increased referral of patients for the investigation and treatment of OSA?

If appropriate services became available for all patients with OSA there would inevitably be cost implications and larger numbers of personnel trained in the area would be required. Training in OSA has been included in the educational programs of all respiratory SpRs for some years, and most recent trainees would be quite able to run services if adequately funded. Thus there is a cohort of young consultants ready and willing to provide such services. The necessary support staff could rapidly be made available as appropriate training courses already exist (Bristol, Stoke, Edinburgh, Brompton, Oxford, BTS), and the BTS has been instrumental in

developing such a course and producing extensive resource material to support it. There have been important developments over recent years that have greatly reduced the costs of investigating and treating OSA [55-58]. Recent estimates of the cost per QALY (quality adjusted life year) vary between only £2,500 and £4,500 depending on the country, and management algorithms used [59-63]. This is without taking into account the savings from vehicle accidents and reduced other health costs. As a comparison with another field within respiratory medicine, QALY estimates for the treatment of non-small cell lung cancer with chemotherapy [64], an intervention supported by NICE through a technology appraisal (number 26, 2001), range between £4,000 and £47,000 (average £15,000).

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